

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ALASKA ELECTRICAL PENSION FUND, et al.,

Plaintiffs

-against-

PHARMACIA CORP., et al.,

Defendants.

03-1519 (AET)

**DECLARATION OF
TIMOTHY C. WANG, M.D. IN
SUPPORT OF DEFENDANTS'
MOTION FOR SUMMARY
JUDGMENT**

I, TIMOTHY CRAGIN WANG, declare, under penalty of perjury, pursuant to 28 U.S.C. § 1746, as follows: I am competent to testify to the statements made herein, and the statements made herein are true and correct based upon my personal knowledge.

I. Background

Education and Experience

1. I am a practicing gastroenterologist and the Dorothy L. and Daniel H. Silberberg Professor of Medicine at Columbia University College of Physicians and Surgeons. I am also the Chief of the Columbia University Medical Center's Division of Digestive and Liver Diseases.

2. I am board certified in both internal medicine and gastroenterology.

3. I received my Bachelor of Arts in Chemistry *summa cum laude* in 1979 from Williams College in Williamstown, Massachusetts and my Doctor of Medicine Degree in 1983 from Columbia College of Physicians and Surgeons, New York, New York. I performed my internship and residency training in Internal Medicine from 1983 through 1986 at Barnes Hospital, Washington University School of Medicine, St. Louis, Missouri. From 1986 through

1990 I was a Research Fellow in Medicine at Harvard Medical School and a Clinical and Research Fellow in Medicine at Massachusetts General Hospital, both in Boston, Massachusetts.

4. I have been a practicing gastroenterologist for over 15 years. From 1991 to 2000 I was an Attending Physician at Massachusetts General Hospital in Boston, Massachusetts. From 2000 through 2004, I was an Attending Physician at UMass Medial Center in Worcester, Massachusetts. Since 2004, I have been an Attending Physician at New York Presbyterian Hospital. At all times during my career, a portion of my practice has been devoted to providing consultation for treatment of patients with gastrointestinal side effects related to the use of non-steroidal anti-inflammatory drugs ("NSAIDs"). I have performed endoscopic procedures on such patients and supervised residents performing endoscopic procedures. In my current position, I presently treat patients on an in-patient basis two months per year where I see dozens of patients with NSAID-related gastrointestinal side-effects and complications.

5. I am also a professor of medicine and have been a guest lecturer and invited speaker at numerous universities and medical centers. Beginning in 1989, I was an Instructor of Medicine at Harvard Medical School, where I was promoted to Assistant Professor of Medicine in 1993 and promoted to Associate Professor of Medicine in 1998. In 2000, I joined the University of Massachusetts Medical School as a tenured Professor of Medicine where I ran the clinical, endoscopic and research programs, and also served as the Director of GI Cancer. In 2004, I joined the faculty at Columbia University College of Physicians & Surgeons where I am currently the Dorothy L. and Daniel H. Silberberg Professor of Medicine. I have also been a Visiting Professor at various universities including Yale University in New Haven, Connecticut, the University of Pennsylvania in Philadelphia, Pennsylvania, and Humboldt University in

Berlin, Germany. I regularly give lectures to students, residents, fellows, and other physicians, including talks regarding NSAID-related gastrointestinal toxicity.

6. As a researcher I have conducted research in the area of gastrin biology, and continue to explore the role of gastrin peptides in diverse diseases, including peptic ulcer disease, gastric cancer and colorectal cancer. Currently, my research program encompasses six major funded projects: (1) the role of *Helicobacter pylori* in gastric cancer pathogenesis; (2) the function and regulation of gastrin; (3) the regulation of histidine decarboxylase gene expression; (4) the function and regulation of trefoil factor 2; (5) gastric cancer stem cells; and (6) the role of stromal cells in the pathogenesis of gastric and liver cancer.

7. From 1996 through 2001, I was an Associate Editor for the professional journal, *Gastroenterology*, and resumed that position on June 1, 2006. From 2003 through 2006, I was an Associate Editor for the American Journal of Physiology (Gastrointestinal Liver Physiology). I have also reviewed for numerous professional journals, including: New England Journal of Medicine, Proceedings for the National Academy of Science, Nature Medicine, Science, Gut, Gastroenterology, American Journal of Gastroenterology, Digestive Diseases and Sciences, Digestion and the Journal of Clinical Investigation. As an editor and reviewer for many years, including the period during which COX-2 selective NSAIDs were researched and developed, I have enjoyed many opportunities to review articles that include historical reviews of NSAID development and write-ups of clinical trials and epidemiological studies relating to NSAIDs.

8. Since 1986, I have been an active member of the American Gastroenterology Association (“AGA”) where I have served on numerous committees within the

association, including the AGA Education Committee, the AGA Council, and the AGA Research Committee. I am currently the Chair of the AGA Future Trends Committee and a member of the AGA Leadership Cabinet. I also belong to other professional societies including the American Board of Internal Medicine (“ABIM”), the American College of Physicians (“ACP”), the American Society for Clinical Investigation (“ASCI”), and the New York Society of Gastrointestinal Endoscopy (“NYSGE”). I am also a member of Phi Beta Kappa and Alpha Omega Alpha, the Honor Medical Society.

9. A copy of my *Curriculum Vitae* and a list of my publications is attached as Exhibit A.

Compensation

10. I am being compensated at my usual rate of \$500 per hour in connection with this proceeding. My compensation is in no way dependent on the opinions I express or on the outcome of the case.

Prior Testimony

11. In the past four years, in addition to the report I submitted in this action in connection with Defendants’ opposition to Plaintiffs’ motion for class certification, I have submitted an expert report, given a deposition and testified at trial, on behalf of the plaintiff, in connection with the following matter: *Pfizer Inc. v. Teva Pharmaceuticals USA, Inc.*, Civil Action No: 04-754 (JCL) (D.N.J.).

II. Materials Considered

12. In forming my opinions and preparing this report, I have reviewed and relied upon the materials cited and listed in this report, as well as the materials listed in Exhibit

B. I have also relied on my extensive knowledge, training and experience as a gastroenterologist in forming the opinions set forth in this report. Reference is also made to certain documents that are attached as exhibits to the accompanying Declaration of William A. Dreier (the “Dreier Decl.”).

III. Subject Matter About Which I Expect to Testify

13. I understand that this is a securities fraud action in which Plaintiffs claim that Defendants made false and misleading statements about the Celecoxib Long Term Arthritis Safety Study (“CLASS”).

14. For purposes of Defendants’ motion for summary judgment, I presently expect to give opinions (and, if requested, am prepared to testify) concerning the public reports of facts concerning the alleged misstatements identified by Plaintiffs regarding CLASS.

15. I may address other matters in response to reports or other evidence offered by Plaintiffs. I reserve the right to supplement or amend my opinions in response to opinions expressed by Plaintiffs’ experts, or in light of any additional evidence, testimony, discovery or other information relating to the aforementioned issues that may be provided to me after the date of this report. In addition, I expect that I may be asked to consider and testify about issues that may be raised by Plaintiffs’ experts in their reports or at trial. In connection with my testimony, I may rely upon certain graphic or demonstrative exhibits that have not yet been prepared.

IV. CLASS

16. For decades before Celebrex® was approved for the U.S. market, doctors recognized that nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with

gastrointestinal side effects, including peptic ulcers, ulcer complications and tolerability issues (such as nausea, abdominal pain and dyspepsia). The medical community, therefore, realized that there was a need for new NSAIDs with improved gastrointestinal (“GI”) safety and tolerability compared to the NSAIDs available to their patients. With that background in mind, Celebrex® was developed and subsequently approved for marketing in the United States in December 1998.¹

17. Based on the acknowledged risk for upper gastrointestinal side effects associated with NSAID use, the FDA has required that approved labeling for prescription NSAIDs include a standard paragraph explaining “that upper GI ulcers, gross bleeding or perforation, caused by NSAIDs, appear to occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year” (the “Standard GI Warning”).²

18. Notwithstanding the evidence demonstrating the superior GI safety profile of Celebrex, the FDA required that the label for Celebrex also include the Standard GI Warning.

19. The CLASS study was commissioned to compare, among other things, the GI safety profile of Celebrex® to that of traditional NSAIDs in order to support Pharmacia’s petition to the FDA for approval of a revised label.

¹ On December 31, 1998, the United States Food and Drug Administration (“FDA”) approved Celebrex® -- the first Cox-2 selective NSAID to be approved in the United States -- for treatment of patients with rheumatoid arthritis and osteoarthritis. The FDA found that Celebrex® was an effective arthritis treatment in placebo and active-controlled clinical trials and demonstrated a significantly lower risk of ulcers detected by endoscopy. See “FDA Talk Paper” *FDA Approves Celebrex for Arthritis* (Dec. 31, 1998). Subsequently, the FDA approved Celebrex® for additional indications.

² See Harold E. Paulus, *FDA Arthritis Advisory Committee Meeting: Serious Gastrointestinal Toxicity of Nonsteroidal Antiinflammatory Drugs; Drug -Containing Renal and Biliary Stones; Diclofenac and Carprofen Approved*, Vol. 31, No. 11, *Arthritis and Rheumatism* 1450-51 (1988); see also *Medical Officer Review* by James Witter, M.D., Ph.D. (“Witter Review”) at 5-6 (Dreier Decl., Ex. 14).

20. The protocol for CLASS specified that Celebrex® would be compared to two commonly used NSAIDs, ibuprofen and diclofenac. The determination of the relative GI safety of Celebrex® versus these other NSAIDs would be made primarily by reference to the incidence of “ulcer complications” – defined, for purposes of the Study, as upper gastrointestinal bleeding, perforation or gastric outlet obstruction in patients with osteoarthritis or rheumatoid arthritis. The incidence of “ulcer complications” was designated as the “primary endpoint” – or, objective – of CLASS. The incidence of a secondary endpoint of “symptomatic ulcers” – defined, for purposes of the Study, as ulcers identified based on upper gastrointestinal symptoms, such as abdominal pain, dyspepsia, nausea, diarrhea or vomiting and confirmed by endoscopic examination of the gastrointestinal tract – was included in the protocol as part of the evaluation of general GI safety. The Study was designed to include approximately eight thousand patients. Approximately four thousand patients would be given Celebrex®, two thousand ibuprofen and two thousand diclofenac. The minimum planned study participation was 6 months.

21. The results of CLASS were presented in an article published in the Journal of the American Medical Association on September 13, 2000, entitled *Gastrointestinal Toxicity With Celecoxib vs Nonsteroidal Anti-inflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis - The CLASS Study: A Randomized Controlled Trial* (the “JAMA Article”) (Dreier Decl., Ex. 2).

22. The JAMA Article reported that Celebrex failed to meet the primary endpoint in that the study did not demonstrate that there were statistically significantly fewer ulcer complications in the Celebrex treatment group than in the comparator treatment groups. However, the JAMA Article reported that, according to various other measures, Celebrex demonstrated superiority to the comparator NSAIDs. Specifically, based on the first six months

of data from the Study, there were statistically significantly fewer complicated and symptomatic ulcers as compared to the pooled NSAID comparators. Dreier Decl., Ex. 2.

23. I understand that Plaintiffs' complaint in this action criticizes the JAMA Article on the grounds that Defendants misrepresented the results of the CLASS Study (1) by using 6 months worth of data and not reporting on the longer-term data that was available; (2) by reporting a combined endpoint consisting of ulcer complications (the "primary endpoint") and symptomatic ulcers (a "secondary endpoint"); (3) by not following the prespecified plan for statistical analysis of the primary endpoint which called for (i) an analysis of the Celebrex v. ibuprofen and diclofenac, combined, and then (ii) an analysis of Celebrex v. ibuprofen and of Celebrex v. diclofenac, individually (but only if Celebrex was significantly superior based on (i)); and (4) because "[a]nalyzing the CLASS Study data pursuant to the original protocol, meaning 12 and 15 months of data compared head-to-head and in combination for ulcer-related complications, Celebrex does not offer greater GI safety than traditional NSAIDs." Dreier Decl., Ex. 1 ¶ 46.

24. I disagree with such criticism and it is my opinion that the analysis offered in the JAMA Article is not misleading, and represents a valid interpretation and presentation of the CLASS data.

25. Nevertheless, I have been asked to assume, for the purposes of this report and for the sake of argument, that the results of CLASS, as presented in the JAMA Article, were misrepresented, and to offer my opinion as to when sufficient facts to reveal these alleged misrepresentations were publicly known. My opinion is that sufficient facts to reveal the alleged misrepresentations were publicly known no later than February 6, 2001, when the FDA posted to

its website the “Briefing Document” submitted by Pharmacia setting forth its analysis of CLASS and reports by two medical officers employed by the FDA (the “FDA Medical Officers”) and a statistician employed by the FDA (the “FDA Statistician”), who analyzed the full CLASS data submitted to the FDA (the “FDA Staff Review Documents”).

V. The “sNDA” And FDA Arthritis Advisory Committee

26. Pharmacia’s application to the FDA to remove the Standard GI Warning is technically known as a “Supplemental New Drug Application” or “sNDA.” The Arthritis Advisory Committee, a committee of outside experts appointed by FDA, was tasked with evaluating the results of CLASS and making a recommendation to the FDA regarding the requested label change. In advance of the Advisory Committee meeting, which was held February 7, 2001, Pharmacia submitted a “briefing document,” setting forth its analysis of the results of CLASS (the “Briefing Document”) (Dreier Decl. Ex. 12).³

27. The Briefing Document presented the CLASS data: (1) using six months of data (as in the JAMA Article) and (2) using data from the entire study period.

28. As a basis for using six months of data, the Briefing Document explained that data after six months was suspect and not statistically meaningful because of disproportionately high withdrawal of patients in the NSAID arms for GI adverse events other than the primary endpoint of ulcer complications:

The GI safety data presented are for the six-month treatment timepoint based on the analysis of risk factors prespecified in the protocol. In brief, a disproportionate withdrawal of patients at high

³ Technically, the Briefing Document was submitted by G.D. Searle & Co. (“Searle”), which I understand is affiliated with Pharmacia. Accordingly, for purposes of this affidavit any references to Pharmacia include Searle.

risk of an ulcer complication from the entire study was observed after six months (depletion of susceptibles). Additionally, a significantly greater withdrawal of patients on diclofenac for GI intolerance occurred during the initial six months of the study. The withdrawal of patients for GI intolerance prematurely removed a group at high risk for ulcer complications and symptomatic ulcers from the diclofenac treatment arm (informative censoring).

Briefing Document (Dreier Decl., Ex. 12) at 28.⁴

29. FDA Medical Officers and an FDA Statistician reviewed the CLASS data and presented their analyses to the Arthritis Advisory Committee for consideration. Dr. James Witter, an FDA Medical Officer, submitted a “Medical Officer Review” (Dreier Decl., Ex. 14), Dr. Lawrence Goldkind, an FDA Medical Officer, submitted a “Medical Officer’s Gastroenterology Advisory Committee Briefing Document” (the “Goldkind Review”) (Dreier Decl., Ex. 13) and Dr. Hong Laura Lu, an FDA Statistician, submitted a “Statistical Reviewer Briefing Document for the Advisory Committee” (the “Lu Review”) (Dreier Decl., Ex. 15) (collectively, the “FDA Staff Review Documents”). The Briefing Document and the FDA Staff Review Documents were made publicly available on February 6, 2001, when they were posted to the FDA website. They remain available there today.⁵

30. On February 7, 2001, the FDA Arthritis Advisory Committee held a public hearing at which representatives of Pharmacia and FDA staff (Medical Officers) made presentations to the committee.

⁴ Ibuprofen users had a significantly higher rate of symptomatic ulcers, necessitating the withdrawal of study participants at high risk for developing a complicated ulcer.

⁵ See <http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1.htm>.

31. Each of the alleged misrepresentations set forth in Paragraph 23, above (summarizing ¶ 46 of the Complaint), was discussed in the Briefing Document and the FDA Staff Review Documents, and during the Arthritis Advisory Committee public hearing.

The Duration Of CLASS

32. Plaintiffs contend that Defendants misrepresented the duration of the CLASS Study because “[t]he CLASS study trial did not last six months as stated. Instead, the Celebrex versus ibuprofen trial lasted 15 months and the Celebrex versus diclofenac trial lasted 12 months.” Dreier Decl., Ex. 1 ¶ 46. This information was publicly known as early as April 17, 2000, and, in any event, no later than February 6, 2001.

33. Pharmacia’s initial press release, issued on April 17, 2000, regarding the CLASS results, stated that the CLASS Study was “an approximately 13 month” study. Dreier Decl., Ex. 3 at 2. This information was repeated in various publications, such as the April 24, 2000 edition of the “Pink Sheet,” an industry newsletter covering the Pharmaceuticals industry (Dreier Decl., Ex. 6 at 1-2), and two April 17, 2000 articles that were reported on the Dow Jones newswire. *See* Dreier Decl., Exs. 4-5.

34. The Briefing Document and the FDA Staff Review Documents, made public on February 6, 2001, also clearly identified the duration of the CLASS Study and the time periods relevant to Pharmacia’s interpretation of the data. *See* Briefing Document (Dreier Decl., Ex. 12) at 18, 28, 45; Goldkind Review (Dreier Decl., Ex. 13) at 12, 14-16, 23-24; Witter Review (Dreier Decl., Ex. 14) at 8, 48; Lu Review (Dreier Decl., Ex. 15) at 1, 5, 8.

35. In addition, comments made by Pharmacia representatives during the Arthritis Advisory Committee public hearing also made clear that the CLASS Study lasted longer than six months. *See* Dreier Decl., Ex. 21 (excerpts of hearing transcripts).

Alleged Expansion Of The Primary Endpoint

36. Plaintiffs contend that Defendants misrepresented the results of CLASS because “after the trials were complete, defendants added symptomatic ulcers to the comparison criteria in order to improve Celebrex’s relative performance.” Dreier Decl., Ex. 1 ¶ 46(c).

37. It was well understood long before the JAMA Article was published, however, that Celebrex failed to demonstrate statistically significant superiority to ibuprofen and diclofenac based on the primary endpoint of CLASS. For example, in an April 18, 2000 report entitled *Positive Results of Celebrex CLASS Trial Released*, Morgan Stanley Dean Witter reported that, “Celebrex did not reach statistically significant superiority on the primary endpoint of ulcer complications.” Dreier Decl., Ex. 9 at 2. This information was similarly reported in the April 24, 2000 edition of the Pink Sheet. Dreier Decl., Ex. 6 at 2.

38. Moreover, the JAMA Article disclosed that Celebrex failed to meet the primary endpoint. *See* JAMA Article (Dreier Decl., Ex. 2) at 1254 (“the rate for ulcer complications did not differ”). Further, in an editorial commenting on the results of CLASS, published in JAMA contemporaneously with the JAMA Article, the authors noted that “even though the combined incidence of symptomatic ulcers . . . associated with celecoxib was significantly lower than with the comparator drugs, careful examination of the data shows that the rate of ulcer complications alone, the primary end point of the study, was not.” David R. Lichtenstein, M.D. and M. Michael Wolfe, M.D., *COX-2-Selective NSAIDs, New and*

Improved?, Vol. 284, No. 10 J. of Am. Med. Ass'n 1297, 1297-99 (Sept. 13, 2000) (Dreier Decl., Ex. 49).

39. The FDA Staff Review Documents also discussed that Celebrex failed to meet the primary endpoint and that the use of a combined endpoint of ulcer complications and symptomatic ulcers was a post-hoc analysis. *See* Goldkind Review (Dreier Decl., Ex. 13) at 21, 41, 52; Lu Review (Dreier Decl., Ex. 15) at 9, 6.

Alleged Failure To Follow The Prespecified Statistical Analysis

40. Plaintiffs allege that Defendants misrepresented CLASS by not reporting the results of CLASS in accordance with the prespecified plan for statistical analysis of the results, which called for (i) an analysis of the Celebrex v. ibuprofen and diclofenac, combined, and then (ii) an analysis of Celebrex v. ibuprofen and of Celebrex v. diclofenac, individually (but only if Celebrex was significantly superior based on (i)). According to Plaintiffs, the protocol specified that Celebrex “would only be found superior . . . if both comparisons, [Celebrex vs. diclofenac and Celebrex vs. ibuprofen], were statistically significant and in favor of Celebrex.” Dreier Decl., Ex. 1 ¶ 46.

41. Plaintiffs’ criticism, however, was publicly discussed in the Goldkind Review, published on the FDA website on February 6, 2001. *See* Dreier Decl., Ex. 13 at 7. Moreover, the protocol called for the primary endpoint (1) to be analyzed at the combined NSAID level and (2) only if the difference were statistically significant to proceed to specific comparisons of ibuprofen and diclofenac. As fully disclosed in the JAMA Article, the primary endpoint was not met and therefore the protocol did not call for comparisons with specific

comparators. Nor did the protocol prescribe a methodology for conducting the secondary analyses.

The Alleged Absence Of Any Safety Advantage According To The CLASS Protocol

42. Plaintiffs contend that Defendants misrepresented the results of CLASS because the JAMA Article did not disclose that if the data is analyzed “pursuant to the original protocol, meaning 12 and 15 months of data compared head-to-head and in combination for ulcer-related complications, Celebrex does not offer greater GI safety than traditional NSAIDs.” Dreier Decl., Ex. 1 ¶ 46. Plaintiffs’ criticism was publicly disclosed no later than February 6, 2001, when it was discussed in the Witter Review. *See* Dreier Decl., Ex. 14 at 48, 82.

43. In addition, comments made by Pharmacia representatives and FDA representatives during the Arthritis Advisory Committee public hearing also made clear that, according to the protocol, Celebrex did not show any statistically significant difference over the comparators. *See* Dreier Decl., Ex. 21.

Conclusions

44. In my opinion, the Briefing Document and the FDA Staff Review Documents that were posted on the FDA website, as well as the public statements made during the FDA Arthritis Advisory Committee hearing, publicly disclosed each of the alleged misrepresentations regarding the results of CLASS identified by Plaintiffs. Most of the information that Plaintiffs claim was concealed in fact was publicly disclosed as early as April 2000. In addition to the evidence discussed above, my opinion is confirmed by the fact that news outlets and securities analysts published reports that reviewed and analyzed the materials posted on the FDA website and discussed at the FDA Arthritis Advisory Committee public

hearing, and, accordingly, discussed the very facts that are alleged to have been misrepresented and/or not disclosed. *See, e.g.*, February 7, 2001 J.P. Morgan Securities analyst report entitled *FDA Review of Celebrex More Negative Than Expected – Panel Could Be Controversial* (Dreier Decl., Ex. 16); Brian Reid, *Pharmacia Hasn't Shown Celebrex Safety Benefit, FDA Review Says*, Bloomberg News, Feb. 6, 2001 (Dreier Decl., Ex. 17).

45. Moreover, at the conclusion of the Arthritis Advisory Committee hearing, the Committee publicly disagreed with Pharmacia's conclusions that the CLASS Study demonstrated the superior GI safety profile of Celebrex. The Committee concluded that CLASS did not demonstrate the superiority of Celebrex over NSAIDs because Celebrex had not met the primary endpoint and recommended to the FDA that the gastrointestinal warning not be removed from the Celebrex label. The Arthritis Advisory Committee's conclusion was widely reported in securities analyst reports and the general press. *See* Dreier Decl., Exs. 23-41. It should be noted, however, that the FDA did not fully follow the Arthritis Advisory Committee's recommendation, and ultimately approved a label change showing the results in CLASS at nine months, including both the primary endpoint of ulcer complications and the combined endpoint of symptomatic ulcers and ulcer complications. *See* "FDA Talk Paper" entitled *Labeling Changes for Arthritis Drug Celebrex* (June 7, 2002) (Dreier Decl., Ex. 22); Celebrex June 2002 Label (Dreier Decl., Ex. 50).

Dated: May 29, 2007



Timothy Cragin Wang, M.D.

EXHIBIT A

CURRICULUM VITAE (UPD. 3/08/06)

Name: Timothy Cragin Wang, M.D.

Address: 455 Central Park West, Apartment #11C
New York, NY 10025

Date of Birth: March 27, 1957

Place of Birth: Allentown, Pennsylvania

Education:

1975: John Burroughs Preparatory School, Ladue, Missouri
1979 B.A. Williams College, Williamstown, Massachusetts
1983 M.D. Columbia College of Physicians and Surgeons, New York, New York

Postdoctoral Training:

Internships and Residencies:

1983-1986 Intern and Resident in Internal Medicine,
Barnes Hospital, Washington
University School of Medicine, St. Louis, Missouri

Research Fellowships:

1986-1989 Research Fellow in Medicine, Harvard Medical School
1986-1989 Clinical and Research Fellow in Medicine, Massachusetts General
Hospital, Boston, Massachusetts

Licensure and Certification:

1987 Massachusetts License Registration No. 55632
2004 New York License No. 233070-1

Academic Appointments:

1989 Instructor of Medicine, Harvard Medical School
1993 Assistant Professor of Medicine, Harvard Medical School
1998 Associate Professor of Medicine, Harvard Medical School
1999 Professor of Medicine (with tenure), University of Massachusetts Medical
School
2004 Assistant Adjunct Professor of Medicine,
Columbia University College of Physicians & Surgeons
2005 Dorothy L. and Daniel H. Silberberg Professor of Medicine
Columbia University College of Physicians & Surgeons

Hospital Appointments:

1989-1991	Clinical Assistant in Medicine, Massachusetts General Hospital
1991	Assistant in Medicine, Massachusetts General Hospital
1994	Assistant Physician, Massachusetts General Hospital
1998	Associate Physician, Massachusetts General Hospital
	Associate Division Chief, Massachusetts General Hospital
2000	Chief, Gastroenterology Division, Director of GI Cancer, University of Massachusetts Medical School
2004	Chief, Digestive and Liver Diseases Director of GI Cancer Columbia University Medical Center

Awards and Honors:

1979	B.A., summa cum laude
1983	M.D. (AOA)
1988	AGA Senior Research Fellow Award
1993	AGA Funderberg Gastric Cancer Award
1998	Election to American Society of Clinical Investigation (ASCI)
1999	Steven Krane Lectureship for Outstanding Young Investigator in the MGH Department of Medicine
2000	Viktor Mutt Medal in Gut Hormone Research
2001	Gladys Smith Martin Chair in Gastrointestinal Cancer
2004	Election to Association of American Physicians (AAP)
2005	Silberberg Chair in Medicine, Columbia P&S

Major Committee Assignments:

Hospital	
1993	Committee on Research, MGH
1993	Subcommittee for Research Animal Care/Studies, MGH
1998	Steering Committee, Gastrointestinal Unit, MGH
1999	Academic Governing Council, Department of Medicine, MGH
2000	Appointments and Promotions Committee, UMass Med School
2000	Member of Cancer Center Search Committee, UMass Medical School
2002	Board Member of Cancer Center Programs Leaders at UMass Medical School
2003	Member of Endoscopy Working Group, UMass Medical School
2003	Member of Pediatric GI Search Committee, UMass Medical School
2004	Department of Medicine Executive Council, Columbia P&S
2005	Member of Radiation Oncology Search Committee, Columbia P&S

National Committee Assignments:

1996-1998	AGA By-Laws Committee
1999-2002	AGA Education Committee
2001-2005	AGA Council, Hormones & Receptors Section
2002-2004	AGA Research Committee
2003	AGA Nominating Committee
2003-2004	Director, AGA 2004 Spring Postgraduate Course (SPGC)
2003-2004	AGA Strategic Planning Committee
2003-5	AGA GRG Committee
2004-2005	AGA Research Policy Committee
2005-2008	Chair, AGA Future Trends Committee

Memberships in Professional Societies:

1979	Phi Beta Kappa
1983	Alpha Omega Alpha
1983-	American Medical Association
1986-	American Gastroenterology Association (AGA)
1986-	American Board of Internal Medicine (ABIM)
1986-	American College of Physicians (ACP)
1998	American Society for Clinical Investigation (ASCI)
2001	American Physiological Society (APS)
2002	American Society for Biochemistry and Molecular Biology (ASBMB)
2003	Crohn's & Colitis Foundation of America (CCFA)
2004	Association of American Physicians (AAP)
2005	New York Society of Gastrointestinal Endoscopy (NYSGE)

Editorial Experience:

1996-2001	Associate Editor, Gastroenterology
2003-2007	Associate Editor, Am. J. Physiol. (<i>Gastrointest Liver Phys</i>)
2006-2010	Associate Editor, Gastroenterology

Journals Reviewed For:

1. Nature Medicine
2. Science
3. New England Journal of Medicine
4. Proceedings for the National Academy of Science
5. EMBO J
6. Journal of Clinical Investigation
7. Endocrinology
8. Cancer Research
9. FEBS Letters
10. Biochemistry Journal
11. FASEB Journal
12. Hepatology

13. Gut
14. Gastroenterology
15. American Journal of Physiology
16. Journal of Cell Physiology
17. Regulatory Peptides
18. American Journal of Gastroenterology
19. Cell Growth & Differentiation
20. Digestive Diseases and Sciences
21. Digestion

Major Research Interests:

1. Regulation of histidine decarboxylase gene expression
2. Role of gastrin in growth and colon cancer
3. The role of cyclin D1 in oncogenesis
4. Mouse models Helicobacter pylori and gastric cancer
5. Function and regulation of trefoil factor 2 (TFF2/SP)
6. Regulate of innate immunity
7. Stem cells and cancer

RESEARCH FUNDING:

CURRENT FUNDING:

NIH RO1CA120979

Funding agency: NIH NCI
Title: Stem cells and gastric cancer
Principal investigator: Timothy C. Wang
Dates of Award: 3/06 to 2/11

NIH RO1 DK 48077

Funding agency: NIH NIDDK
Title: The regulation of histidine decarboxylase gene expression
Principal investigator: Timothy C. Wang
Dates of Award: 6/04 to 6/09

NIH RO1 DK52778

Funding agency: NIH NIDDK
Title: Function and regulation of gastrin
Principal investigator: Timothy C. Wang
Dates of Award: 03/01/04 to 02/28/09

NIH RO1 CA93405

Funding agency: NIH NCI
Title: Mouse models of gastric cancer
Principal Investigator: Timothy C. Wang

Dates of Award: 4/1/01 to 3/31/06

NIH RO1 DK58889-01

Funding agency: NIH NIDDK

Title: Function and regulation of spasmolytic polypeptide/TFF2

Principal Investigator: Timothy C. Wang

Dates of Award: 3/1/01 to 2/28/06

NIH RO1 AI51405-01

Funding agency: NIH NAID

Title: Heat shock proteins and *Helicobacter pylori* pathogenesis

Principal Investigator: Evelyn Kurt-Jones; Co-PI: Timothy C. Wang

Dates of Award: 4/01/02 – 3/31/07

RECENT PAST FUNDING: Not included.

POST-DOCTORAL FELLOWS PAST:

<u>NAME</u>	<u>TRAINING PERIOD</u>	<u>RESEARCH PROJECT</u>	<u>CURRENT POSITION</u>
Michael Hoecker	1993-1996	Role of Gastrin in Chromogranin a Regulation	Associate Professor of Medicine, Charite Med School, Humboldt University
Zhensheng Zhang	1993-1996	Human HDC Promoter	Assistant Professor of Medicine Memorial Medical School, NIH
Ted Koh	1994-1997	Role of Gastrin in Gastro-Intestinal Development	Assistant Professor of Medicine Syracuse Hospital, New York
Robert Henihan	1996-1998	Regulation of the HDC Promoter by somatostatin	Wilmington Gastroenterology Associates, North Carolina
Raktima Raychowdhury	1996-2000	Gastrin Regulation of the HB-EGF Gene	Research Associate Professor of Medicine, Harvard University
John Fleming	1997-2003	Expression and Regulation of Histidine Decarboxylase	Research Assistant Professor, Institute of Molecular Medicine Lisboa, Portugal
Woo Kyu Jean	1997-1998	Regulation of TFF2	Assistant Professor of Medicine Samsung University, Seoul, Korea
Clemens Bulitta	1998-2000	Regulation of gastrin and TFF2	Siemens Medical Solutions Health Services GmbH Erlangen, Germany
Rocchina Colucci	1997-1999	Regulation of HDC promoter	Research Assistant Professor

			Faculty of Medicine, Pisa Univ
James Farrell	1998-2001	Generation and Characterization of TFF2 Deficient Mouse	Assistant Professor of Medicine UCLA School of Medicine
John McLaughlin MD, PhD	1998-1999	Gastrin Regulation of the HB-EGF Gene	Assistant Professor of Medicine Manchester University, England
Abhijit Chaklader PhD	2000-2002	Molecular Characterization of Human Rotaviruses Isolated from Clinical Cases	Staff Scientist, Harvard Medical School, UMass Medical School
Chung-Wei Lee MD	2000-2001	Regulation of Mouse TFF2 Promoter Activity	PhD. Student, Massachusetts Institute of Technology (MIT)
Guanglin Cui MD	2001-2003	The Role of Cytokines in Gastritis	University of Tromso Tromso, Norway
SeonHee Lim MD, PhD.	2002-2003	Regulation of TFF2 Gene Expression	Assistant Professor of Medicine Kang Nam Hospital, Seoul, Korea
Alfred Chi PhD	2001-2004	Regulation of TFF2	Founder of biotech company
Shi Lei PhD	2001-2004	Regulation Of Gastrin Gene Expression	Postdoc with Dr. Steve Reppert Neurobiology, UMass

CURRENT POST-DOCS

Wandong Ai, PhD	2002-Present	Regulation of HDC Promoter Activity	Associate Research Scientist Columbia P&S
Shigeo Takaishi MD, PhD	2002-Present	Mouse Model of Gastric Cancer	Associate Research Scientist Columbia P&S
Alexander Dubeykovskiy, PhD	2003-Present	Progastrin and Cancer	Associate Research Scientist Columbia P&S
Zina Dubeykovskaya, PhD	2004-Present	Trefoil Family Factor 2	Post-doctoral Research Scientist Columbia P&S
Shuiping Tu, MD, Ph.D	2004-Present	Mouse Models of Gastric Cancer	Post-doctoral Research Scientist Columbia P&S
Iva Smirnova, MD, PhD	2004-present	Gastric Progenitor Cells	Post-doctoral Research Scientist Columbia P&S
Tomoyuki Okumura MD, PhD	2005-Present	Stem Cells and Cancer	Post-doctoral Research Scientist Columbia P&S
Frederic Marrache MD, PhD	2005-Present	Models of Pancreatic Cancer	Post-doctoral Research Scientist Columbia P&S
Sheng-Wen Wang MD, PhD	2005-Present	Inflammation and cancer	Post-doctoral Research Scientist Columbia P&S

Principal Clinical and Hospital Service Responsibilities:

1991- Attending Physician, Medical Service, Massachusetts General Hospital
 2000- Attending Physician, UMass Medical Center
 2004- Attending Physician, New York Presbyterian Hospital

Major Administrative Responsibilities:

1992: Director of GI Unit Research Journal Club
 1993: Co-Director, Course on Techniques in Molecular and Cellular Biology
 1995: Director of Transgenic Core Laboratory, CSIBD
 1996: Director of GI Unit Research Seminar Series
 1998: Director of Partner's dyspepsia disease management program
 1998: Associate Chief, Gastrointestinal Unit, MGH
 2000: Chief, Gastrointestinal Division, UMass Medical
 2004: Chief, Gastroenterology Division, Columbia University Medical School

Teaching Experience:

1991-2000 Visit on the Gastrointestinal Service
 1992-2000 Visit on the Bigelow Medical Service
 1993-2000 Co-director of the IBD Center Molecular Biology Course
 1993-2004 Lecturer at Harvard Postgraduate course in Gastroenterology, Infectious Diseases, and Surgery
 1998-2000 Lecturer in CME program: AMIL Physicians from Brazil
 2000-2004 Attending on the UMass Medicine and GI services
 2000-2004 Co-director of GI Pathophysiology course, UMass Medical School
 2001-2005 Thesis committee Tox/Path for M.I.T.
 2002, 2004, 2005 AGA, Academic Skills Workshop

Invited Speaker:

1991 University of Pennsylvania
 1992 University of Michigan
 1993 Boston University
 Peptide Growth Factor Conference, Vail, Colorado
 1994 Visiting Lecturer, CURE, UCLA
 1995 Tufts University/New England Medical Center
 Massachusetts Institute of Technology
 1996 GI Cancers: Biology and Genetics, Reston, VA
 1997 Gastrin Conference, Liverpool, UK
 MIT, Division of Toxicology
 1998 Visiting Lecturer, Univ. of Michigan
 Visiting Lecturer, UTMB
 Visiting Lecturer, Medical College of Georgia
 K-Club, DDW, New Orleans

Yamanouchi Symposium, Tokyo Japan
 Visiting Professor, University of Cincinnati
 1999 Keystone Symposium on GI Cancer
 Chugai Symposium, DDW, Orlando
 Visiting Professor, National University, Taiwan
 Visiting Lecturer, Mount Sinai Medical Center
 2000 Visiting Lecturer, University of Massachusetts
 Visiting Lecturer, Brigham and Woman's Hospital
 Visiting Lecturer, Emory University
 Visiting Lecturer, Massachusetts Institute of Technology
 Visiting Lecturer, Merck Corporation, Pennsylvania
 Visiting Professor, Humboldt University, Berlin, Germany
 Victor Mutt Lectureship, Cairns, Australia
 External Scientific Advisory Board, Washington Univ. Nutrition
 Center
 2001 Visiting Professor, University of Pennsylvania
 Visiting Professor, University of Connecticut
 Visiting Professor, Yale University
 Invited Speaker, Worcester Medical Center/St. Vincent's Hospital
 Invited Speaker, APDW, Sydney, Australia
 Invited Speaker, Conference on gastric cancer, Astra-Zeneca,
 Waltham, MA
 Invited Speaker, Keio and Kyoto Universities, Japan
 Invited Speaker, FASEB, Kalispell, Montana, July 2001
 Invited Speaker, FASEB, Ottawa, Quebec, Canada, October 2001
 Invited Speaker, University of Toronto
 Invited Speaker, 3rd International Conference on Trefoils April
 2002 Invited Speaker, Pacific Basin Group on Gastroduodenal Disorders
 Meeting
 Invited Speaker, University of Pennsylvania Postgraduate Course
 Invited Speaker, Yale University School of Medicine
 2003 Invited Speaker, Beth Israel Deaconess Hospital, Boston
 Salmon Visiting Professor of Medicine: Vanderbilt University
 Invited Speaker: "Biology of gastrointestinal bleeding", Yale
 University
 Invited Speaker: "*Helicobacter pylori* and gastric cancer",
 Columbia College of Physicians and Surgeons, NY.
 Invited Speaker: "*Helicobacter pylori* and gastric cancer", Duke
 University Medical Center
 Invited Speaker: *Helicobacter* and gastric cancer, Astra-Zenneca
 International Consensus Conference, Stockholm, Sweden.
 Grand Rounds speaker: *H. pylori*: Update 2003, St. Vincent's
 Medical Center, Worcester, MA.

- Grand Rounds speaker: *H. pylori*: Update 2003, Holy Family Hospital, Methuen, MA.
- Invited speaker: Infection and inflammation: the origins of epithelial cancers, Beth Israel Deaconess Hospital, Boston, MA
- 2004 Invited Speaker: Massachusetts General Hospital, "Trefoil factor 2: non-epithelia expression and the origin of epithelial cancers"
- Invited Speaker: UCLA, VA Healthcare System, CURE "Helicobacter and Gastric Cancer"
- Invited Speaker, Dana Farber Cancer Center, "Helicobacter, Inflammation and Gastric Cancer"
- Invited Speaker at Massachusetts General Hospital, GI Grand Rounds "H pylori and Gastric Cancer" in the Isselbacher Library
- Invited Speaker: 15th International Symposium of Regulatory Peptides, "Non-processed gastrins: effects, mechanisms of action and pathophysiological relevance", Toulouse, France
- Pediatric GI Grand Rounds, "*Helicobacter* and gastric cancer", Columbia University Medical Center
- Invited lecture: Cornell Medical School, GI Grand Rounds, "*Helicobacter pylori* and gastric cancer." Columbia College of P&S, Medical Grand Rounds, "*H. pylori* and gastric cancer."
- Invited speaker, 4th International Conference on Trefoil factors, Strasbourg, France. "Trefoil factor-2 (TFF2): non-epithelial expression and possible role in immune regulation."
- 2005
- January Lecture to GI fellows at Columbia on "Peptic Ulcer Disease"
- Invited lecture: GI Grand Rounds, "*Helicobacter* and gastric cancer" St. Luke's/Roosevelt Hospital, New York, NY
- March Invited speaker: Stanford University Microbiology, Molecular Oncology Research Seminar, "*Helicobacter pylori* and gastric cancer: anew paradigm for epithelial cancer", Palo Alto, CA
- Invited lecture: GI Grand Rounds, "Helicobacter and gastric cancer: a new paradigm for inflammation mediated neoplasia", Stanford University, Palo Alto, CA
- Invited speaker: Genentec Molecular Oncology Seminar, "Helicobacter pylori and gastric cancer: a new paradigm for cancer stem cells", South San Francisco, CA
- Invited speaker: Washington Hospital Center, Cardiovascular Revascularization Therapies (CRT) 2005 Conference, "Studies suggesting that stem cell might be carcinogenic", Washington, DC
- April Invited speaker: National Cancer Institute Sponsored Workshop on Mucosal Immunosureillance, Inflammation and Cancer, "Inflammation and carcinogenesis", Rockville, MD
- May Invited speaker: John Hopkins School of Medicine Jr. Faculty Research Program IBD Symposium, Management problems in IBD: Immunomodulators, Biologics and Dysplasia. Baltimore, MD

State of the Art Lecture and session co-chair: American Gastroenterological Association Annual Meeting, "Stem cells and cancer", Chicago, IL
 Invited speaker: AGA Postgraduate Course, Digestive Diseases Week 2005, "Gastritis and cancer", Chicago, IL
 Invited speaker: Japanese K-Club, Chicago, IL
 June Invited Lecture: Hematology/Oncology Research Seminar, " ", New York University School of Medicine, New York, NY
 Invited speaker and session chair: 10th US-Japan GI & Liver Meeting in the 21st Century, "Helicobacter and gastric cancer: a new paradigm for epithelial malignancy", Kyoto, Japan
 Sept Invited Speaker: AGA-British Society of Gastroenterology (BSG) Meeting, "Stem cells and GI carcinogenesis", Oxford, England
 Invited Lecture: GI Grand Rounds and Research Seminar, "Helicobacter, inflammation and stem cells: a new paradigm in epithelial cancer", University of Pennsylvania, Philadelphia, PA
 Invited Speaker: World Congress of Gastroenterology, "H pylori, gastritis and gastric cancer: pathologic mechanisms", Montreal, Canada

Conferences Organized:

November 1999: Third International Conference on Gastrin
 September 2002: International Regulatory Peptide Symposium
 May 2004: AGA/GRG Symposium: Stem cells and cancer stem cells.
 May 2004: AGA Spring Postgraduate Course (SPGC)
 October 2004 FASEB conference: Gastrointestinal Response to Injury: Canada 2004
 Planned for 2006: AGA Symposium on "Stem cells in Cancer and Development"

NIH Study Sections:

Ad hoc: Program Projects: 1994, 1996
 NIDDK-C 1999, 2000
 Member: NIDDK-C (6/2000-6/2004)
 NIH Gastrointestinal Cell & Molecular Biology DDK-GCMG (2004-present)

Patents filed:

2002 Diagnosis and treatment of gastrointestinal disease (Role of gastrin isoforms in the susceptibility to gastric atrophy and cancer). US Serial No. 10/257, Filed 10/8/02.
 2003 Origins of gastric cancer (pending).
 2003 Histamine and CCK2/gastrin receptor blockade in the treatment of acid-peptic disease and cancer (pending).

Bibliography

Original Peer-Reviewed Articles:

1. Linday L, Dobkin JF, Wang TC, Butler VP, Shaha JR, Linderbaum J. Digoxin inactivation by gut flora in infants and Children. *Pediatrics*. 1987; 79:544-548.
2. Parsonnet J, Welch K, Compton C, Strauss R, Wang TC, Kelsey P, Ferraro MJ. Simple microbiologic detection of campylobacter pylori. *J Clin Micro*. 1988; 26:948-949.
3. Brand SJ, Wang TC. Gastrin gene expression and regulation in rat islet cell lines. *J Biol Chem*. 1988; 263:16597-16603.
4. Green PHR, O'Toole KM, Slonim D, Wang TC, Weg A. Increasing incidence and excellent survival of patients with early gastric cancer: experience of a United States medical center. *Am J Med*. 1988; 85:658-661.
5. Lee EY, Wang TC, Clouse RE, DeSchryver-Kecsckemeti K. Mucosal thickening adjacent to gastric malignancy: association with epidermal growth factor. *Modern Pathology*. 1989; 2:397-402.
6. Wang TC, Brand SJ. Islet cell specific regulatory domain in the gastrin promoter contains adjacent positive and negative DNA elements. *J Biol Chem*. 1990; 265:8908-8914.
7. Strauss RM, Wang TC, Kelsey PB, Compton CC, Ferraro MJ, Perez-Perez G, Parsonnet J, and Blaser MJ. Association of helicobacter pylori infection with dyspeptic symptoms in patients undergoing gastroduodenoscopy. *Am J Med*. 1990; 89:464-469.
8. Awad JA, Lee EY, Wang TC, Deschryver-Kecsckemeti K, Clouse RE. Effect of mucosal thickening near gastric carcinoma on the endoscopic diagnosis of malignancy. *Dig Dis Sci*. 1990; 35:317-320.
9. Richter JM, Wang TC, Fawaz K, Bynum TE, Fallon D, and Shapleigh C. Practice patterns and costs of hospitalization for upper gastrointestinal hemorrhage. *J Clin Gastro*. 1991; 13:268-273.
10. Shiota G, Rhoads DB, Wang TC, Nakamura T, and Schmidt EV. Hepatocyte growth factor inhibits growth of hepatocellular carcinoma cells. *Proc Natl Acad Sci USA*. 1992; 89:373-377.
11. Wang TC, Brand SJ. Function and regulation of gastrin in transgenic mice: A review. *Yale J. Biol. Med*. 1992; 65:705-713.
12. Wang TC, Bonneir-Weir S, Oates P, Chulak M, Merlino GT, Schmidt EV, Brand SJ. Pancreatic gastrin stimulates islet differentiation of TGF-alpha-induced ductular precursor cells. *J Clin Invest* 1993; 92:1349-1356.
13. Tillotson LG, Wang TC, Brand SJ. Activation of gastrin transcription in pancreatic islet cells by a CACC promoter element and a 70 kDa sequence specific DNA binding protein. *J Biol Chem* January 1994, 269:2234-2240.
14. Jeffrey GP, Babyatsky M, Oates PS, Wang TC, Brand SJ. Spasmolytic polypeptide - an abundant trefoil peptide secreted lumenally from mucous cells in adult and fetal rat stomach. *Gastroenterology* 1994 106:336-345.
15. Shiota G, Wang TC, Nakamura T, Schmidt EV. Hepatocyte growth factor in transgenic mice; effect on hepatocyte growth, liver regeneration, and gene expression. *Hepatology*, April, 1994, 19:962-972.

16. Wang TC, Cardiff RD, Zuckerberg L, Lees E, Arnold A, and Schmidt EV. Mammary hyperplasia and carcinoma in MMTV-Cyclin D1 transgenic mice. *Nature* June 23 1994; 369:669-671.
17. Sharp R, Babyatsky M, Takagi H, Tagerud S, Wang TC, Bockman DE, Brand SJ, and Merlino G. Transforming growth factor alpha can disrupt the normal program of cellular growth and differentiation in the gastric mucosa of transgenic mice. *Development* 121:149-161, 1995.
18. Wang TC, Babyatsky M, Oates PS, Zhang Z, Tillotson L, Chulak MB, Brand SJ, Schmidt EV. The rat gastrin-human gastrin chimeric transgene directs antral G cell specific expression in transgenic mice. *Am. J. Phys.* 268 (Gastrointest. Liver Physiol. 31): G1025-G1036, June, 1995.
19. Haase VH, Wang TC, Schmidt EV, and Bernards A. Normal lymphopoiesis in transgenic mice over-expressing the ltk transmembranous tyrosine kinase. *Transgenics* 1995, 1:487-495.
20. Koh TJ and Wang TC. Molecular cloning and sequencing of the murine gastrin gene. *Biochem. Biophys. Res. Commun.* 1995; 216:34-41.
21. Fox JG, Li X, Cahill R, Andrutis K, Rustgi AK, Odze R, and Wang TC. Hypertrophic gastropathy in *Helicobacter felis* infected wild type C57BL/6 mice and p53 hemizygous transgenic mice. *Gastroenterology* 1996 110:155-166.
22. Höcker M, Zhang Z, Fenstermacher DA, Tagerud S, Chulak MB, Joseph D, and Wang TC. The histidine decarboxylase promoter is regulated by gastrin through a protein kinase C pathway. *Am. J. Physiol.* 270 (Gastrointest. Liver Physiol. 33):G619-G633, 1996.
23. Liang TJ, Reid AE, Xavier R, Cardiff RD, and Wang TC. Transgenic expression of tpr-met oncogene leads to development of mammary hyperplasia and tumors. *J. Clin. Invest.* 97:2872-2877, 1996.
24. Zhang Z, Höcker M, Koh TJ, and Wang TC. The human Histidine Decarboxylase promoter is regulated by gastrin and PMA through a downstream cis-acting element. *J. Biol. Chem.* 271:14188-14197, 1996.
25. Wang TC, Koh TJ, Varro A, Cahill R, Dangler CA, Fox JG, and Dockray GJ. Processing and proliferative effects of human progastrin in transgenic mice. *J. Clin. Invest.* 98:1918-1929, 1996.
26. Höcker M, Koh TJ, Zhang Z, and Wang TC. Regulation of histidine decarboxylase gene expression. *Yale J. Biol. Med.* 1996; 69:21-33.
27. Höcker M, Zhang A, Merchant JL, and Wang TC. Gastrin regulates the human histidine decarboxylase promoter through an AP-1-dependent mechanism. *Am. J. Physiol.* 272 (Gastrointest. Liver Physiol. 35): G822-G830, 1997.
28. Kawamura T, Furusaka A, Koziel MJ, Chung RJ, Wang TC, Schmidt EV, and Liang TJ. Transgenic expression of hepatitis C virus structural proteins. *Hepatology* 1997; 25:1014-1021.
29. Nakagawa H, Wang TC, Togawa K, Zuckerberg L, Odze R, Wilson JB, and Rustgi AK. Overexpression of cyclin D1 in the esophageal epithelium results in dysplasia in transgenic mice. *Oncogene* 1997; 14:1185-1190.

30. Koh TJ, Goldenring JR, Ito S, Mashimo H, Kopin AS, Varro A, Dockray GJ, and Wang TC. Gastrin knockout mice show altered gastric differentiation and decreased colonic proliferation. *Gastroenterology* 113:1015-1025, 1997.
31. Fox JG, Dangler CA, Whary MT, Edelman W, Kucherlapati R, and Wang TC. Mice carrying a truncated Apc gene have diminished gastric epithelial proliferation, gastric inflammation, and humoral immunity in response to *Helicobacter felis* infection. *Cancer Research* 57:3972-3978, September 1997.
32. Höcker M, Zhang Z, Koh TJ, and Wang TC. Mitogen-activated protein kinase pathways mediate the activation of the histidine decarboxylase promoter by gastrin and PMA. *J. Biol. Chem.* 1997; 272:27015-27024.
33. Wharton RH, Wang TC, Graeme-Cook F, Briggs S, and Cole RE. Acute idiopathic gastric dilatation with gastric necrosis in individuals with Prader-Willi syndrome. *Am. J. Med. Sci.* 1997; 73:437-441.
34. Wang TC, Goldenring JR, Ito S, Dangler C, Müller A, Jeon WK, Koh TJ, and Fox JG. C57BL/6 mice deficient in secretory phospholipase A2 show increased apoptosis and altered cellular differentiation after *Helicobacter felis* infection. *Gastroenterology*, 1998; 114:675-689.
35. Höcker M, Rosenberg I, Henihan RJ, Xavier R, Podolsky DK, and Wang TC. Hydrogen peroxide activates the human histidine decarboxylase promoter in AGS gastric cancer cells. *J. Biol. Chem.* 1998; 273: 23046-23054.
36. Höcker M, Raychowdhury R, Plath T, Wu H, O'Connor DT, Wiedenmann B, Rosewicz S, and Wang TC. Sp1 and CREB mediate gastrin-dependent regulation of chromogranin A promoter activity in gastric carcinoma cells. *J. Biol. Chem* 1998; 273:34000-34007.
37. Koh TJ, Dockary GJ, Varro A, Cahill RJ, Dangler CA, Fox JG, and Wang TC. Overexpression of glycine-extended gastrin in transgenic mice results in increased colonic proliferation. *J. Clin. Invest.* 1999; 103: 1119-1126
38. Taupin D, Chyang-Wu D, Jeon W-K, Wang TC, and Podolsky DK. The trefoil gene family are coordinately expressed immediate-early genes: EGF receptor- and MAP kinase-dependent interregulation. *J. Clin. Invest.* 1999; 103: R31-R38.
39. Raychowdhury R, Zhang Z, Höcker M, and Wang TC. Activation of the human histidine decarboxylase promoter by gastrin is mediated by two distinct nuclear factors. *J. Biol. Chem.* 1999 274: 20961-20969.
40. Wang, TC and Dockray GJ. Lessons from genetically engineered animal models. I. Physiologic studies with gastrin in transgenic mice. *Am J. Physiol.* 277 (Gastrointest. Liver Physiol. 40): G6-G11, 1999.
41. Höcker M, John M, Anagnostopoulos I, Buhr HJ, Solimena M, Gasnier B, Henry JP, Wang TC, and Wiedenmann B. Molecular dissection of regulated secretory pathways in human gastric enterochromaffin-like cells: an immunohistochemical analysis. *Histochem Cell Biol* 1999 112:205-214.
42. Fox JG, Dangler CA, Taylor NS, King A, Koh TH, and Wang TC. High salt diet induces gastric epithelial hyperplasia, parietal cell loss, and enhance *Helicobacter pylori* colonization in C57BL/6 mice. *Cancer Research* 1999; 59:4823-4828.
43. Plath T, Höcker M, Riecken EO, Wang TC, Wiedenmann B, and Rosewicz S. Interferon-alpha inhibits chromogranin A promoter activity in neuroendocrine pancreatic cells. *FEBS Letters* 1999; 45:378-382.

44. Wang TC, Dangler C, Chen C, Goldenring JR, Koh TJ, Raychowdhury R, Coffey RJ, Ito S, Varro A, and Fox JG. Synergistic interaction between hypergastrinemia and *Helicobacter* infection in a mouse model of gastric carcinoma. *Gastroenterology* 2000;118:36-47.
45. Singh P, Velasco M, Given R, Wargovich M, Varro A, Wang TC. Mice overexpressing progastrin are predisposed for developing aberrant colonic crypt foci in response to AOM. *American Journal of Physiology - Gastrointestinal & Liver Physiology*. 278:G390-9, 2000.
46. Weffler S, Höcker H, Wang TC, Wiedenmann B, Meyer TF, and Naumann M. *Helicobacter pylori* activates the human histidine decarboxylase promoter through an extracellular-regulated kinase pathway independent of pathogenicity island-encoded virulence factors. *J Biol Chem*. 275:3629-36, 2000.
47. Fox JG, Beck P, Dangler CA, Whary MT, Wang TC, Shi HN, and Anderson CN. Concurrent enteric helminth infection modulates inflammation, gastric immune responses, and reduces *Helicobacter*-induced gastric atrophy. *Nature Medicine* 2000; 6:536-542.
48. Fleming JV and Wang TC. Amino- and carboxy- terminal PEST domains mediate gastrin stabilization of rat L-histidine decarboxylase isoforms. *Mol. Cell. Biol*. 2000; 20:4932-4947.
49. Singh P, Velasco M, Given R, Varro A, and Wang TC. Progastrin expression predisposes mice to development of colon carcinomas and adenomas in response to azoxymethane. *Gastroenterology* 2000;119:162-171.
50. Chen D, Zhao C-M, Dockray GJ, Varro A, van Hoek A, Sinclair NF, Wang TC, and Koh TJ. Glycine-extended gastrin synergizes with gastrin-17 to stimulate acid secretion in gastrin-deficient mice. *Gastroenterology* 2000; 119:756-765.
51. Koh TJ, Bulitta CJ, Fleming JV, Dockray GJ, Varro A, and Wang TC. Gastrin a target of the beta-catenin/TCF-4 growth-signaling pathway in a model of intestinal polyposis. *J. Clin. Invest*. 2000; 106:533-539.
52. Dockray GJ, Varro A, Dimaline R, and Wang TC. "Progastrin-derived peptides and their biological activities." *Annual Review of Physiology* 2001; 63:119-140.
53. Manickan E, Satoi J, Wang TC, Liang TJ. Conditional liver-specific expression of simian virus 40 t antigen leads to regulatable development of hepatic neoplasm in transgenic mice. [Journal Article] *Journal of Biological Chemistry*. 276(17):13989-94, 2001 April 27.
54. Imanishi Y, Hosokawa Y, Yoshimoto K, Schipani E, Mallya S, Papanikolaou A, Kifor O, Tokura T, Sablosky M, Ledgard F, Gronowicz G, Wang TC, Schmidt EV, Hall C, Brown EM, Bronson R, Arnold A. Primary hyperparathyroidism caused by parathyroid-targeted overexpression of cyclin D1 in transgenic mice. [Journal Article] *Journal of Clinical Investigation*. 107(9):1093-102, 2001 May.
55. Höcker M, Cramer T, Rosewicz S, O'Connor DT, Wiedenmann B, and Wang TC. Neuroendocrine specific expression and gastrin-dependent regulation of a chromogranin A-luciferase fusion gene in transgenic mice. *Gastroenterology* 2001;121:43-55.
56. Brembreck FH, Moffett J, Wang TC, and Rustgi AK. The keratin 19 promoter is potent for cell-specific targeting of genes in transgenic mice. *Gastroenterology* 2001; 120:1720-1728.

57. Chung RT, He W, Saquib A, Chawla A, Wang TC, and Schmidt EV. Hepatitis C virus replication is directly inhibited by interferon-alpha in a novel replication system. *Proc Natl Acad Sci USA* 2001; 98:9847-9852.
58. Colucci R, Fleming JV, and Wang TC. "L-histidine decarboxylase decreases its own transcription through downregulation of ERK activity". *Am. J. Physiol.* 2001;281:G1081-1091.
59. Hosokawa Y, Papanikolaou A, Cardiff RD, Yoshimoto K, Bernstein M, Wang TC, Schmidt EV, and Arnold A. In vivo analysis of mammary and non-mammary tumorigenesis in MMTV-cyclin D1 transgenic mice deficient in p53. *Transgenic Research* 2001; 10:471-478.
60. Keates AC, Keates S, Kwon JH, Arseneau KO, Law DJ, Bai L, Merchant JL, Wang TC, Kelly CP. ZBP-89, Sp1, and nuclear factor-kappa B regulate epithelial neutrophil-activating peptide-78 gene expression in Caco-2 human colonic epithelial cells. [Journal Article] *Journal of Biological Chemistry*. 276(47):43713-22, 2001 November 23
61. Gadd M, Pisc C, Branda J, Ionescu-Tiba V, Nikolic Z, Yang C, Wang T, Shackelford GM, Cardiff RD and Schmidt EV. Regulation of cyclin D1 and p16INK4A is critical for growth arrest during mammary involution. *Cancer Res.* 2001; 61:8811-9.
62. Farrell JJ, Taupin D, Koh TJ, Chen D, Zhao CM, Podolsky DK, and Wang TC. TFF2/SP-deficient mice show decreased gastric proliferation, increased acid secretion, and increased susceptibility to NSAID injury. *J. Clin. Invest.* 2002 109: 193-204
63. Clerc P, Leung-Theung-Long S, Garnier A, Wang TC, Dockray GJ, Vaysse N, Pradayrol L, Fourmy D, and Dufresne M. Expression of CCK2 receptors in the murine pancreas: Proliferation, transdifferentiation of acinar cells and neoplasia. *Gastroenterology* 2002; 122:428-439.
64. Fox JG, Sheppard BJ, Dangler CA, Whary MT, Ihrig M, and Wang TC. Germ-line p53-targeted disruption inhibits Helicobacter-induced premalignant lesions and invasive gastric carcinoma through downregulation of Th1 proinflammatory responses. *Cancer Research* 2002 62:696-702.
65. Bulitta CJ, Fleming JV, Raychowdhury R, Taupin D, Rosenberg I, and Wang TC. Autoinduction of the trefoil factor 2 (TFF2) promoter requires an upstream cis-acting element. *Biochem Biophys Res Commun.* 2002 Apr 26;293(1):366-74
66. Shea T, Wang TC, and Ferris T. A program to improve the management of patients on long term acid suppression. *Journal of Clinical Outcome Management* 2002; 9(6):312-318.
67. Kirton CM, Wang TC, Dockray GJ. Regulation of parietal cell migration by gastrin in the mouse. *Am J Physiol Gastrointest Liver Physiol* 2002 ; 283:G787-G793.
68. Raychowdhury R, Schäfer G, Rosewicz S, Wiedenmann B, Wang TC and Höcker M. Interaction of Early Growth Response Protein 1 (Egr-1) with Sp1 and CREB at a proximal response element is critical for gastrin-dependent activation of the chromogranin A promoter. *Mol Endocrinol.* 2002 Dec;16(12):2802-18..
69. Raychowdhury R, Bulitta CJ, Fleming JV, McLaughlin J, and Wang TC. Identification and characterization of a third gastrin response element (GAS-RE) in the human histidine decarboxylase gene promoter. *Biochem Biophys Res Commun.* 2002 Oct 11;297(5):1089-95.

70. Jacobson BC, Ferris TG, Shea TL, Mahlis EM, Lee T, and Wang TC. Who is using chronic acid-suppression therapy and why? *American Journal of Gastroenterology* 2003; 98:51-58.
71. Fleming JV and Wang TC. The production of 53-55kDa isoforms is not required for rat L-histidine decarboxylase (HDC) activity. *J Biol Chem.* 2003 Jan 3;278(1):686-94.).
72. Fox JG, Rogers AB, Ihrig M, Taylor NS, Whary MT, and Wang TC. *Helicobacter pylori* associated gastric cancer in INS-GAS mice is gender-specific. *Cancer Research* 2003; 63:942-950.
73. Ottewell PD, Watson AJM, Wang TC, Dockray GJ, and Pritchard DM. Progastrin Stimulates Murine Colonic Epithelial Mitosis After DNA Damage. *Gastroenterology.* 2003 May;124(5):1348-57.
74. Fox JG, Wang TC, Rogers AB, Poutahidis T, Ge Z, Taylor N, Dangler CA, Israel DA, Drishna U, Gaus K, and Peek RM. Host and Microbial Constituents Influence *Helicobacter pylori*-Induced Cancer in a Murine Model of Hypergastrinemia. *Gastroenterology.* 2003 Jun;124(7):1879-90
75. Lee JR, Baxter TM, Yamaguchi H, Wang TC, Goldenring JR, Anderson MG. Differential protein analysis of Spasmolytic Polypeptide Expressing Metaplasia using laser capture microdissection and 2-Dimensional Difference Gel Electrophoresis. *Appl Immunohistochem Mol Morphol* 2003;11:188-193.
76. Song DH, Rana B, Wolfe JR, Crimmins G, Choi C, Wang TC, Pestell RG, Albanese C, Wolfe MM. Gastrin induced gastric adenocarcinoma growth is mediated through cyclin D1. *Am J Physiol Gastrointest Liver Physiol.* 2003 Jul;285(1):G217-22. Epub 2003 Feb 26.
77. Khan ZE, Wang TC, Cui G, Chi AL, Dimaline R. Transcriptional regulation of the human trefoil factor, TFF1, by gastrin1. *Gastroenterology.* 2003 Aug;125(2):510-21.
78. Mahata SK, Mahapatra NR, Mahata M, Wang TC, Kennedy BP, Ziegler MG, O'Connor DT. Catecholamine secretory vesicle stimulus-transcription coupling in vivo: demonstration by a novel transgenic promoter/photoprotein reporter, and inhibition of secretion and transcription by the chromogranin A fragment catestatin. *J Biol Chem.* 2003 Aug 22;278(34):32058-67. Epub 2003 Jun 10.
79. Dhar DK, Wang TC, Maruyama R, Udagawa J, Kubota H, Fuji T, Tachibana M, Ono T, Otani H, Kohno H, and Nagasue N. Expression of cytoplasmic TFF2 is a negative prognostic factor in gastric cancer. *Lab Invest.* 2003 Sep;83(9):1343-52.
80. Boushey RP, Abadir A, Flamez D, Baggio LL, Li Y, Berger V, Marshall BA, Finegood D, Wang TC, Schuit F, and Drucker DJ. Hypoglycemia, defective glucagon secretion, but normal islet mass in mice with a targeted disruption of the gastrin gene. *Gastroenterology.* 2003 Oct;125(4):1164-74.
81. McLaughlin JT, Sinclair NF, Colucci R, Raychowdhury R, Wang TC and Koh TJ. PACAP regulates the histidine decarboxylase promoter via dual signaling mechanisms. *Am J Physiol Gastrointest Liver Physiol.* 2004; 286(1): G51-9.
82. Ai W, Liu Y, Langlois M, Wang TC. Kruppel-like factor 4 (KLF4) represses histidine decarboxylase gene expression through an upstream Sp1 site and downstream gastrin responsive elements. *J Biol Chem.* 2004 Mar 5;279(10):8684-93. Epub 2003 Dec 10.

83. Koh TJ, Field JK, Varro A, Liloglou T, Fielding P, Cui G, Houghton J, Dockray GJ, Wang TC. Glycine-extended gastrin promotes the growth of lung cancer. *Cancer Res.* 2004 Jan 1;64(1):196-201.
84. Sinclair NF, Ai W, Raychowdhury R, Bi M, Wang TC, Koh TJ, McLaughlin JT. Gastrin Regulates the Heparin Binding Epidermal-like Growth Factor Promoter Via a PKC/EGFR dependent mechanism. *Am J Physiol Gastrointest Liver Physiol.* 2004; 286:G992-9.
85. Fleming JV, Fajardo I, Langlois MR, Sanchez-Jimenez F, Wang TC. The C-terminus of rat L-histidine decarboxylase specifically inhibits enzymic activity and disrupts pyridoxal phosphate-dependent interactions with L-histidine substrate analogues. *Biochem J.* 2004; 381(Pt 3):769-78.
86. Fleming JV, Sanchez-Jimenez F, Moya-Garcia AA, Langlois MR, Wang TC. Mapping of catalytically important residues in the rat L-histidine decarboxylase enzyme using bioinformatic and site-directed mutagenesis approaches. *Biochem J.* 2004 Apr 15;379(Pt 2):253-61.
87. Chi AL, Lim SH, Wang TC. Characterization of a CCAAT-enhancer element of trefoil family factor 2 (TFF2) promoter in MCF-7 cells. *Peptides* 2004; 25:839-47.
88. Pradeep A, Sharma C, Sathyanarayana P, Albanese C, Fleming JV, Wang TC, Wolfe MM, Baker KM, Pestell RG, Rana B. Gastrin-mediated activation of cyclin D1 transcription involves beta-catenin and CREB pathways in gastric cancer cells. *Oncogene.* 2004 Apr 29;23(20):3689-99.
89. Mandell L, Moran AP, Cocchiarella A, Houghton JM, Taylor N, Fox JG, Wang TC, Kurt-Jones EA. Intact gram-negative *Helicobacter hepaticus*, *Helicobacter pylori*, and *Helicobacter felis* bacteria activate innate immunity via Toll-like receptor-2 not Toll-like receptor 4. *Infect Immun* Nov. 2004 ; 72:6446-54.
90. Nomura S, Baxter T, Yamaguchi H, Vartapetian AB, Fox JG, Lee JR, Wang TC, Goldenring JR. Spasmolytic polypeptide expressing metaplasia to preneoplasia in H. felis-infected mice. *Gastroenterology.* 2004 Aug;127(2):582-94.
91. Lei S, Dubeykovskiy A, Chakladar A, Wojtukiewicz L, Wang TC. The murine gastrin promoter is synergistically activated by TGF-beta/Smad and Wnt signaling pathways. *J Biol Chem.* 2004; 279:42492-502.
92. Cui G, Koh TJ, Chen D, Zhao CM, Dockray GJ, Varro A, Rogers AB, Fox JG, Wang TC. Overexpression of glycine-extended gastrin alters the development of peptic ulcer and preneoplasia in the mouse stomach. *Cancer Research* 2004; 64:8160-6.
93. Houghton JM, Stoicov C, Nomura S, Rogers AB, Carlson J, Li H, Cai X, Fox JG, Goldenring JR, and Wang TC. Gastric cancer originating from bone marrow derived cells. *Science* 2004; 306:1568-71.
94. Kurt-Jones EA, Sandor F, Ortiz Y, Bowen GN, Counter SL, Wang TC, Finberg RW. Use of murine embryonic fibroblasts to define Toll-like receptor activation and specificity. *J. Endotoxin Res.* 2004;10(6):419-24.
95. Ottewell PD, Varro A, Dockray GJ, Watson AJM, Kirton CM, Wang TC, Dimaline R, Pritchard DM. The C-terminal 26 amino acid residues of progastrin are sufficient for stimulation off mitosis in murine colonic epithelium in vivo. *Am J Physiol Gastrointest Liver Physiol.* 2005 Mar;288(3):G541-9. Epub 2004 Oct 14.

96. Nomura S, Yamaguchi H, Leys C, Wang TC, Lee JR, Goldenring JR. Alterations in gastric mucosal lineages in gastrin deficient mice induced by acute oxyntic atrophy. *Am J Physiol Gastrointest Liver Physiol*. 2005 Feb;288(2):G362-75.
97. Cai X, Carlson J, Stoicov C, Li H, Wang TC, Houghton J. *H. felis* eradication restores normal architecture and inhibits gastric cancer progression in the C57BL/6 mouse. *Gastroenterology* 2005 June;128(7):1937-52.
98. Takaishi S, Cui G, Frederick DM, Carlson JE, Houghton J, Varro A, Dockray GJ, Ge Z, Whary MT, Rogers AB, Fox JG, and Wang TC. Synergistic inhibitory effects of gastrin and histamine receptor antagonists on *Helicobacter*-induced gastric cancer. *Gastroenterology* 2005 June;128(7):1965-83.
99. Ferrand A, Bertrand C, Portolan G, Cui G, Carlson J, Pradayrol L, Fourmy D, Dufresne M, Wang TC, Seva C. Signaling pathways associated with colonic mucosa hyperproliferation in mice overexpressing gastrin precursors. *Cancer Res*. 2005 Apr;65(7):2770-7.
100. Dhar DK, Wang TC, Tabara H, Tonomoto Y, Maruyama R, Tachibana M, Kubota H, Nagasue N. Expression of trefoil factor family members correlates with patient prognosis and neoangiogenesis. *Clin Cancer Res*. 2005 Sep 15;11(18):6472-8.
101. Chakladar A, Dubeykovskiy A, Wojtukiewicz LJ, Pratap J, Lei S, Wang TC. Synergistic activation of the murine gastrin promoter by oncogenic Ras and beta-catenin involves SMAD recruitment. *Biochem Biophys Res Commun*. 2005 Oct 14;336(1):190-6.
102. Ogawa M, Nomura S, Varro A, Wang TC, Goldenring JR. Altered metaplastic response of waved-2 EGF receptor mutant mice to acute oxyntic atrophy. *Am J Physiol Gastrointest Liver Physiol*. 2005 Nov 23; [Epub ahead of print]
103. Rogers AB, Taylor NS, Whary MT, Stefanich ED, Wang TC, Fox JG. *Helicobacter pylori* but not high salt induces gastric intraepithelial neoplasia in B6129 mice. *Cancer Res*. 2005 Dec 1;65(23):10709-15.
104. Ai W, Liu Y, Wang TC. Yin Yang 1 (YY1) represses histidine decarboxylase (HDC) gene expression with SREBP-1a in part through an upstream Sp1 site. *Am J Physiol Gastrointest Liver Physiol*. 2005 Dec 15; [Epub ahead of print]
105. Ottewill PD, Duckworth CA, Varro A, Dimaline R, Wang TC, Watson AJM, Dockray GJ, Pritchard DM. Gastrin signals via the CCK-2 receptor to increase murine intestinal crypt regeneration following injury. *Gastroenterology* 2006 (in press).
106. Kurt-Jones EV, Cao L, Cerny A, Bowen G, Takaishi S, Chi A, Whary M, Fox JG, Wang TC. Trefoil factor family 2 (TFF2) is expressed by immune cells and is a major regulator of inflammation and the IL-1 α pathway. *Infect. Immun.* (submitted).
107. McCaig C, Duval C, Hemers E, Steele I, Pritchard DM, Przemeck S, Dimaline R, Ahmed S, Bodger K, Kerrigan DD, Wang TC, Dockray GJ, Varro A. The role of matrix metalloproteinase (MMP)-7 in redefining the gastric microenvironment in response to *H. pylori*. *Gastroenterology* (submitted) 2006.
108. Cui G, Takaishi S, Ai W, Florholmen J, Koh TJ, Houghton J, Wang TC. Gastrin-induced apoptosis contributes to the development of gastric atrophy. *Lab. Invest*. 2006 (resubmitted).
109. Pagliocca A, Khan Z, Wang TC, Dimaline R, Varro A, Dockray GJ. Gastrin-dependent parietal cell maturation: role of ezrin. *J. Cell Sci* (submitted).

110. Kobayashi M, Lee H, Gilmartin T, Schaffer L, Head S, Takaishi S, Wang TC, Nakayama J, and Fukuda M. Gene expression profile during inflammation-carcinoma sequence in the mouse gastric mucosa infected by *Helicobacter felis*. 2006 (submitted).
111. Takaishi S, Wang TC. Gene expression profiling in a mouse model of *Helicobacter*-induced gastric cancer. *Int J Cancer* (submitted) 2006.
112. Ai W, Zheng H, Liu Y, and Wang TC. Tip60 functions as a potential corepressor of KLF4 in regulation of HDC promoter activity. *Mol Cell Bio* (submitted) 2006.
113. Varro A, Kenny S, Hemers E, McCaig C, Przemeck S, Wang TC, Pritchard DM. Increased gastric expression of MMP-7 in hypergastrinaemia and significance for maintenance of stroma in ECL cell carcinoid tumors. *Gut* (submitted) 2006.

Reviews, editorials and chapters:

1. Brand S, Godley J, **Wang T**, and Simon B. Regulation of gastrin gene transcription: cell-specific, developmental and physiological aspects. *Neuropeptides and their receptors*. 1990; 29:95-104.
2. Brand SJ, Babyatsky MW, Bachwich D, Demediuk B, Tillotson L, **Wang TC**. Regulation of gastrin gene transcription. In: *Gastrin*, J.H. Walsh ed., Raven Press 1993:73-90
3. Brand SJ, Babyatsky M, Bachwich D, Tillotson L, **Wang T**. Molecular approaches to the study of gut peptides. In: *Gut Peptides: Biochemistry and Physiology*. J Walsh and G Dockray, eds. Raven Press, 1994, pp. 11-32
4. **Wang TC**. "The biology of gastric cancer," in *Gastrointestinal Cancers: Biology, Diagnosis, and Therapy*, edited by Anil K. Rustgi. Lippincott-Raven Publishers 1995, pp 243-259
5. **Wang TC**. "The history of the mouse: Part I," in *Gastroenterology*, 1997; 113:1431
6. Fox JG and **Wang TC**. *Helicobacter* and liver disease [Review] *Italian Journal of Gastroenterology and Hepatology*. 29:5-10, 1997
7. **Wang TC** and Fox JG. "*Helicobacter pylori* and gastric cancer: Koch's postulates fulfilled," in *Gastroenterology*, 1998; 115:780-783
8. **Wang, TC**. "No time at all," *Gastroenterology*, December, 1998 115:1315
9. Fox JG and **Wang TC**. "Overview of *Helicobacter pylori*", From: *Infectious Causes of Cancer: Targets for Intervention*. 2000. Edited by J.J. Goedert. Humana Press Inc., Totowa, NJ, pp. 371-388
10. Farrell JJ. **Wang TC**. Acid Related Disease: Biology and Treatment. [Journal Article] *Gastroenterology*. 117(3):743-744, 1999 September
11. **Wang TC**. "Follow the money." *Gastroenterology*. 118:819, 2000

12. Fox JG, **Wang TC**. Reply to ""The 'African enigma' - another explanation"" [Journal Article] *Nature Medicine*. 6(12):1297-1298, 2000 December
13. Fox JG, **Wang TC**, Nagler-Anderson C. The African enigma: the parasite's perspective. [Letter] *Gut*. 49(1):156-7, 2001 Jul
14. Fox JG, **Wang TC**. Helicobacter pylori--not a good bug after all! [letter; comment]. [Comment. Editorial] *New England Journal of Medicine*. 345(11):829-32, 2001 Sep
15. Koh TJ and **Wang TC**. "Tumors of the stomach" in Sleisenger & Fordtran's Gastrointestinal & Liver Disease, 7th edition, edited by M Feldman, LS Friedman, and M Sleisenger, WB Saunders Co., 2002, ppp. 829-855.
16. Fox JG and **Wang TC**. *Helicobacter pylori* infection: pathogenesis. Current Opinion in Gastroenterology 2002; 18 (1):15-25.
17. Houghton J, Fox JG, **Wang TC**. Gastric cancer: laboratory bench to clinic. J Gastroenterol Hepatol. 2002 Apr;17(4):495-502.
18. **Wang TC**, Goldenring, JR. Inflammation intersection: gp130 balances gut irritation and stomach cancer. Nat Med. 2002 Oct;8(10):1080-2.
19. Zivny J, **Wang TC**, Yantiss R, Kim KH, Houghton J. Role of therapy or monitoring in preventing progression to gastric cancer. J Clin Gastroenterol. 2003 May-Jun;36 (5):S50-60.
20. Farrell J and **Wang TC**. "The biology of gastric cancer," in Gastrointestinal Cancers, edited by AK Rustgi and J. Crawford. W.B. Saunders 2003, pp. 299-320.
21. Li H, Stoicov C, Cai X, **Wang TC**, Houghton J. Helicobacter and gastric cancer disease mechanisms: host response and disease susceptibility. Curr Gastroenterol Rep. 2003 Dec;5(6):459-67.
22. **Wang TC**. "Gastrin transgenes and gastric cancer." Gastrin in the New Millenium, edited by J. L. Merchant, A.M.J. Buchan, and T.C. Wang. CURE Foundation, Los Angeles, CA 2004, pp. 235-252.
23. Houghton JM and **Wang TC**. "Tumors of the stomach." in Sleisenger & Fordtran's Gastrointestinal & Liver Disease, 8th edition, edited by M Feldman, LS Friedman, and M Sleisenger, WB Saunders Co., 2005, (in press).
24. Houghton J, **Wang TC**. Helicobacter pylori and gastric cancer: a new paradigm for inflammation-associated epithelial cancers. Gastroenterology. 2005 May;128(6):1567-78. Review.
25. Ferrand A, **Wang TC**. Gastrin and cancer: A review. Cancer Lett. 2005 Jul 26; [Epub ahead of print]
26. Ai W, Takaishi S, Wang TC, Fleming J. Regulation of histidine decarboxylase (HDC) and its role in carcinogenesis. Prog in Nucleic Acid Research 2006 (in press).

Abstracts:

All abstracts listed below were presented at the Annual Meetings of the representative societies.

1. Dangler C. A, Fox J.G., **Wang TC**. *Helicobacter felis*-infected C57BL/6 mice develop altered mucin phenotype consistent with intestinal metaplasia. *Gastroenterology*. April 1998; 114:4: G2390.
2. Singh P, Velasco M, Given R, Owlia A, Wargovich M, **Wang TC**. High levels of Progastrin significantly increase premalignant changes in colonic mucosa of mice in response to the chemical carcinogen, AOM. *Gastroenterology*. April 1998; 114:4: G2810.
3. Koh T, Dockray GJ, Varro A, Chen D, and **Wang TC**. The targeted disruption of the gastrin gene in mice results in decreased proliferation of the stomach and colon in response to refeeding. *Gastroenterology*. April 1998; 114:4: G3644.
4. Taupin D, Jeon WK, **Wang TC**, Podolsky DE. EGF receptor- and map kinase-dependent inter-regulation within the immediate early trefoil gene family. *Gastroenterology*. April 1998; 114:4: G3731.
5. Bate GW, Varro A, Dimaline R, **Wang TC**. Enterochromaffin-like (ECL) cell function in transgenic mice expressing gastrin in pancreatic β cells. *Gastroenterology*. April 1998; 114:4: G4611.
6. Chen D, Koh, T, Zhao CM, Hakanson R, **Wang TC**. ECL Cells and gastric acid secretion in gastrin-deficient mice. *Gastroenterology*. April 1998; 114:4: G4646.
7. Henihan RDJ, Colucci R, Zhang Z, **Wang TC**. Somatostatin type 2 receptor (SSTR2) inhibition of histidine decarboxylase (HDC) transcription is not mediated through a phosphatase pathway in the human gastric cancer cell line, AGS-B. *Gastroenterology*. April 1998; 114:4: G4702.
8. Hocker M, Plath T, Wiedenmann B, Riecken EO, Rosewicz S, **Wang TC**. Camp-dependent signaling pathways regulate the human histidine decarboxylase promoter through activation of MAPK/ERK-cascades in gastric cancer cells. *Gastroenterology*. April 1998; 114:4: G4705.
9. Hocker M, Raychowhury R, Wu, H, O'Connor DT, Riecken EO, Rosewicz S, **Wang, TC**. SP1 and CREB mediate Gastrin-dependent regulation of chromogranin a promoter activity. *Gastroenterology*. April 1998; 114:4: G4706
10. Raychowdhury R, Zhang, Z, **Wang TC**. Activation of human histidine decarboxylase (HDC) gene transcription by gastrin is mediated by two distinct nuclear factors. *Gastroenterology*. April 1998; 114:4: G4800.
11. Chen D, **Wang TC**, Dockray G, Varro A, Zhao CM, Hakansson R, Koh, T. Glycine-extended gastrin synergizes with Gastrin 17 to stimulate acid secretion in gastrin deficient mice. *Gastroenterology*. April 1999; 116:4:2:G0587.

12. Farrell JJ, Taylor N, Fox JG, **Wang TC**. Human secretory phospholipase A2 is a helicobacter pylori inducible gene. *Gastroenterology*. April 1999; 116:4:2: G0682.
13. Path T, Hocker M, **Wang TC**, Riecken EO, Wiedenmann B, Rosewicz S. INTERFERON – Inhibits Chromogranin A Promoter Activity in Pancreatic Neuroendocrine Cancer Cells. . *Gastroenterology*. April 1999; 116:4:2:G1852.
14. Velasco M, **Wang TC**, Given R, Wargovich, M, Sigh P. Non-amidated gastrins, but not amidated gastrins function as co-carcinogens in an azoxymethane (AOM) induced colon cancer model. *Gastroenterology*. April 1999; 116:4:2:G2302.
15. **Wang TC**, Dangler CH, Chen D, Goldenring JR, Koh TJ, Raychowdhury R, Coffey R, Ito S, Varro A, Dockray GJ, Fox JG. Hypergastrinemia leads to atrophy and invasive gastric cancer in transgenic mice. *Gastroenterology*. April 1999; 116:4:2: G2314.
16. Chen D, Zhao CM, Koh T, Hakansson R, **Wang TC**. ECL cell hypotrophy but not hypoplasia in antrectomized rats and gastrin deficient mice. *Gastroenterology*. April 1999; 116:4:2: G2613.
17. Colucci R, Fleming JV, Raychowdhury R, **Wang TC**. Feedback inhibition of histidine decarboxylase is mediated by decreased activity of gas-re elements. *Gastroenterology*. April 1999; 116:4:2: G2619.
18. Hocker M, Path T, Du M, Merchant JL, Raychowdhury R, **Wang TC**, Weidenmann B, Rosewicz S. Gastrin regulates the chromogranin a promoter through mek-1-and ERK-dependent phosphorylation of SP1 and CREB. *Gastroenterology*. April 1999: 116:4:2: G2670.
19. Hocker M, Cramer T, Rosewicz S, Wiedenmann B, **Wang TC**, Clin, BF. Neuroendocrine-specific expression and gastrin-dependent regulation of a chromogranin a-luciferase fusion gene in transgenic mice. *Gastroenterology*. April 1999; 116:4:2: G2671.
20. Koh T, Dockray G, Varro A, Cahill RJ, Dangler DA, Fox JG, **Wang TC**. Overexpression of glycine-extended gastrin in transgenic mice results in increased colonic proliferation. *Gastroenterology*. April 1999; 116:4:2: G2699
21. McLaughlin J, **Wang TC**, Koh, TJ. Pacap regulates the histidine decarboxylase promoter via dual (PKA/PKC) signaling pathways. *Gastroenterology*. April 1999; 116:4:2: G2735.
22. McLaughlin J, Koh TJ, **Wang TC**. Gastrin activates the human heparin binding-EGF promoter via a PKC/MAP kinase-dependent pathway in AGS cells. . *Gastroenterology*. April 1999; 116:4:2: G2736.
23. Raychowdhury R, **Wang TC**. Cloning of a novel transcription factor which mediates Gastrin responsiveness by the human histidine decarboxylase (HDC) promoter. *Gastroenterology*. April 1999; 116:4:2: G2785.
24. Raychowdhury R, McLaughlin J, **Wang TC**. Identification and characterization of a new gastrin response element (GAS-RE3) in the human histidine decarboxylase gene promoter. *Gastroenterology*. April 2000; 118:4: 1020.
25. Fox JG, Dangler CA, Beck PL, **Wang TC**, Whary MT, Shi HN, Anderson CN. Intestinal helminth infection modulates inflammation and reduces gastric atrophy in a mouse model of helicobacter infection. *Gastroenterology*. April 2000; 118:4: 1226.
26. Brembeck FH, **Wang TC**, Rustigi AK. The keratin 19 promoter is potent for cell-specific targeting of genes in transgenic mice. *Gastroenterology*. April 2000; 118:4: 1615.

27. Koh TJ, Bulitta CJ, Fleming JV, Dockray GJ, Varro A, **Wang TC**. Gastrin is a downstream target of the b-catenin/TCF-4 signaling pathway which mediated growth in the APC model of intestinal polyposis. *Gastroenterology*. April 2000; 118:4: 2385.
28. Jacobson BC, Ferris TG, Shea TL, Greenberg P, **Wang TC**. Who is using chronic acid-suppression therapy and why? *Gastroenterology*. April 2000; 118:4: 2514.
29. Fleming JV, Sussman JS, Colucci R, Bulitta CJ, **Wang TC**. Gastrin preferentially stabilizes l-histidine decarboxylase (HDC) isoforms that have been processed at both the amino-and carboxy-terminal ends. *Gastroenterology*. April 2000; 118:4: 2882.
30. Chow A, Zhang R, **Wang TC**. Gastrin regulates AE2 CL/HCO₃ exchanger in gastric cells. *Gastroenterology*. April 2000; 118: 4: 3059.
31. Colucci R, Taccaa MD, Fleming JV, **Wang TC**. Overexpression of histidine decarboxylase decreases its own transcription through down-regulation of ERK activity. *Gastroenterology*. April 2000; 118: 4: 3060.
32. Bulitta CJ, Raychowdhury R, Taupin D, Wang TC, MacCallum P. TFF2 and PMA induced TFF2 regulation requires a specific cis-acting element: insights into molecular initiation of restitution. *Gastroenterology*. April 2000; 118: 4: 3694.
33. Chen D, Wang TC, Zhao CM, Hakanson R, Koh TJ. Possible mechanism of synergizing effect of gly-cine-extended Gastrin on Gastrin-17-induced acid secretion in Gastrin knockout mice. *Gastroenterology*. April 2000; 118: 4: 3882.
34. Beck PL, Xavier RJ, Kosaka T, Dangler CA, **Wang TC**, Fox JG. Defining the role of lymphocytes and sialyl-lewis-x (SLE^x) in helicobacter in induced gastric injury. *Gastroenterology*. April 2000; 118:4: 3995.
35. Farrell JJ, Xavier, R, Taylor, N, Fox, JG, **Wang, TC**. Secretory phospholipase A2 promoter regulation by gastrin and helicobacter pylori using cell culture and a green fluorescent protein transgenic mouse model. *Gastroenterology*. April 2000; 118:4: 4005.
36. Boushey RP, Tavares W, Yusta B, Koh TJ, **Wang TC**, Drucker DJ. Essential roles of the Gastrin and glucagons genes in the response to experimental murine colitis. *Gastroenterology*. April 2000; 118: 4: 4338.
37. Taupin D, Farrell, JJ, Koh TJ, Podolsky DK, **Wang TC**, MacCallum P. Generation and characterization of a Spasmolytic polypeptide (TFF2) knockout mouse. *Gastroenterology*. April 2000; 118: 4: 4348.
38. Colucci R, Biandizzi C, **Wang TC**, Lasagna N, Lazzeri G. Role of Cyclooxygenase-2 in the Proliferative Activity of Gastrin on Human Colon Cancer Cells. *Gastroenterology*. April 2001; 120:5:198.
39. Fox JG, Sheppard BJ, Dangler CA, Whary MT, Ihrig M, **Wang TC**. Mutant p53 Inhibits Helicobacter-induced Premalignant Lesions Through Downregulation of Th1 Proinflammatory Responses. *Gastroenterology*. April 2001; 120:5: 460.
40. Khan ZE, **Wang TC**, Varro A, Dimaline R. Transcriptional Regulation of the TFF1 Gene by Gastrin. *Gastroenterology*. April 2001; 120:5:534:
41. Chow A, Zhang R, **Wang TC**. Gastrin Regulates Transcription of AE2b Chloride-Bicarbonate Exchanger via E Box-Binding Proteins. . *Gastroenterology*. April 2001; 120:5:549.
42. Farrell JJ, Taupin D, Koh TJ, Podolsky DK, **Wang TC**. Targetted Gene Deletion of Murine SP.TFF2 Results in Decreased Gastric Proliferation, Increased Basal Acid Secretion and Increased Susceptibility to NSAID Injury. *Gastroenterology*. April 2001; 120:5:744.

43. Clerc P, Leung-Theung-long S, Bouisson M, **Wang TC**, Dockray DJ, Vaysse N, Fourmy D, Durense, M. Overexpression of CCK2/Gastrin Receptors in the Murine Pancreas Results in Growth of the Pancreas, Transdifferentiation of Acinar Cells and Neoplasia. April 2001; 120:5:955.
44. Rana B, Choi C, Crimmins GM, **Wang TC**, Pestell RG, Albanese C, Wolfe M. Cyclin D1 Mediates the Trophic Properties of Gastrin in Gastric Adenocarcinoma. Gastroenterology. April 2001; 120:5: 3583.
45. Chow A, Zhang R, **Wang TC**. Mapping of Critical Elements for High Basal Transcription of AE2b Chloride-Bicarbonate Exchanger in Gastric Cells and Tissues. Gastroenterology. April 2001; 120:5:3774.
46. Sheppard BJ, Ihrig M, Taylor NS, **Wang TC**, Fox JG. Gastric Responses of *Helicobacter pylori*-Infected INS-GAS Mice to a High-Salt Diet Are Gender-Specific. Gastroenterology. April 2002; 122:4:A-1.
47. Baxter TM, Yamaguchi H, **Wang TC**, Fox JG, Anderson MG, Goldenring JR, Lee J. Gene Microarray and Proteomic Analysis of Spasmolytic Polypeptide Expressing Metaplasia (SPEM) in Laser capture Microdissected Cells from H. felis- Infected Mice. Gastroenterology. April 2002; 122:4: A-171.
48. Chow A, Zhang R, **Wang TC**. Gastric Expression of AE2b C1/HC03 Exchanger by an Upstream Palindromic Region. Gastroenterology. April 2002; 22:4: A-521.
49. Yamaguchi H, Lee JR, Rio MC, **Wang TC**, Goldenring JR. Etiology of Carcinoma in pS2 Knockout Mice. Gastroenterology. April 2002;122:4: A-235.
50. Pritchard, D, Ottewell PD, Watson AJM, **Wang TC**, Dockray GJ. Progastrin Stimulates Murine Colonic Ephithelial Mitosis after DNA Damage. Gastroenterology. April 2002; 122:4: A-684.
51. Takaishi S, Cui G, Frederick D, Carlson J, Houghton J, **Wang TC**. Gene expression profiling in a mouse model of gastric cancer. Gastroenterology 2003; 124:4: A-142.
52. Cui G, Houghton JM, Finkel N, Carlson J, **Wang TC**. IFN-gamma infusion induces gastric atrophy, Metaplasia and dysplasia in the absence of Helicobacter infection- a role for immune response in Helicobacter disease. Gastroenterology. April 2003;124: 4:A-19.
53. Wojtukiewicz L, Chakladar A, **Wang TC**. Oncogenic Regulation of Gastrin Gene Expression: Three Signals for a Peptide's Fate. Gastroenterology. April 2003; 124: 4: A-105.
54. Cui G, Koh TJ, Chen D, Zhao CM, Dockray GJ, Varro A, Fox JG, **Wang TC**. Overexpression of Cyclic-Extended Gastrin Maintains Acid Secretion and Prevents the Development of Preneoplasia in the Stomach Via Reducing Parietal Cell Lost in Transgenic Mice. Gastroenterology. April 2003; 124: 4: A-141.
55. Chi AL, Lim S, Guanglin C, Takaishi S, Fleming JV, Lee C, **Wang TC**. Gastrin Transcriptionally Regulates Trefoil Family Factor 2. Gastroenterology. April 2003; 124: 4: A-451.
56. Lei S, Chakladar A, Wojtukiewicz L, **Wang TC**. Gastrin Expression is Regulated by the Interplay of TGF-beta/Smads and Wnt Pathways. Gastroenterology. April 2003; 124: 4: A-472.
57. Ai W, Liu Y, Langlois M, **Wang, T**. Yin Yang Represses Histidine Decarboxylase Promoter Activity in Part Through an Upstream Sp1 Binding Site. Gastroenterology. April 2004; 126:4: A-34.

58. Takaishi S, Cui G, Carlson JE, Varro A, Dockray GJ, Ge Z, Whary MT, Rogers AB, Fox JG, **Wang, TC**. Synergistic Inhibitory Effects on Gastrin and Histamine Receptor Antagonists in Helicobacter-Induced Gastric Carcinogenesis. *Gastroenterology*. April 2004; 126:4: A-81.
59. Nomura S, Yamaguchi H, Ogawa M, **Wang TC**, Goldenring JR. Alterations in Gastric Mucosal Lineages Induced by Acute Oxynitic Atrophy in Normal and Gastrin Knockout Mice. *Gastroenterology*. April 2004; 126:4: A-92.
60. Normura S, Baxter T, Yamaguchi H, Vartapetian AB, Fox JG, Lee JR, **Wang TC**, Goldenring JR. Spem-Related Genes Including Prothymosin-Alpha Are Expressed in Gastric Dysplasia in H. Felis-Infected Mice. *Gastroenterology*. April 2004; 126:4: A-96.
61. Ferrand A, Bertrand C, Portolan G, Cui G, Carlson J, Pradayrol L, Fourmy D, Dufrense M, **Wang T**, Seva C. Signaling Pathways Contributing to Colonic Mucosa Hyperproliferation in Transgenic Mice Overexpressing Progastrin or Glycine-Extended Gastric.
62. Cui G, Takaishi S, Ai W, Carlson JE, Frederick DM, **Wang TC**. Gastric Cell Apoptosis Induced by Gastrin Stimulation is Mediated by CCK-B/Gastrin Receptors and Histamine-2 Receptors. *Gastroenterology*. April 2004; 126:4:A-273.
63. Rogers AB, Taylor NS, Xu S, **Wang TC**, Fox JG. Gastric Intraepithelial Neoplasia in Helicobacter Pylori Infected B6129 Mice is Not Promoted BY a High Salt Diet. April 2005;110:4:A19.
64. Takaishi S, Ai W, Tu S, Dubeikovskiy A, Dubeikovskaya Z, Smirnova I, Tran AV, Betz KS, **Wang TC**. Gastrin and Helicobacter-Infection Regulate Claudin gene Expression in the Tight Junction of Gastric Epithelial Cells: Claudin-7 Is a Novel Intestinal Metaplasia and Gastric Neoplasia Marker in Helicobacter-Infected Mice Stomach. April 2005;113:4:A-20.
65. Ai W, Liu Y, Takaishi S, Tu S, **Wang TC**. Tip60 Functions As a Potential Co-Repressor of Klf4 in Regulation of Human Histidine Decarboxylase Promoter. April 2005;395:4:A-57.
66. Tu S, Cui G, Takaishi S, Tran AV, Frederick DM, Carlson JE, Kurt-Jones E, **Wang TC**. Overexpressiion of Human Interleukin-1 beta in Transgenic Mice Results in Spontaneous Gastric Inflammation and Carcinogenesis. April 2005;421:4:A-62.
67. Ogawa M, Nomura S, **Wang TC**, Goldenring JR. Spasmolytic Polypeptide Expressing Metaplasia (sperm) in Spasmolytic Polypeptide (sp/tff2) Deficient Mice. April 2005;879:4:A-142.

EXHIBIT B

Documents Considered

Legal Pleadings

- Consolidated Amended Complaint for Violation of the Federal Securities Laws, dated October 27, 2003
- Plaintiffs' Memorandum of Law in Support of Plaintiffs' Motion for Class Certification, dated April 3, 2006

FDA Documents

- Transcript of the February 7, 2001 FDA Arthritis Advisory Committee meeting

CLASS Study Documents

- CLASS Study Protocols N49-98-22-035; N49-98-12-102
- A Plan Of The Final Analysis For Celecoxib Incidence Of Clinically Significant UGI Adverse Events vs. Ibuprofen & Diclofenac In OA Or RA (Studies N49-98-22-035 and N49-98-12-102), dated October 7, 1999

All other sources cited in report and exhibits.